Pharmacological identification of cholinergic receptor subtypes in Drosophilia

Acetylcholine (ACh) is an abundant neurotransmitter and neuromodulator in many species. In Drosophila melanogaster ACh is the neurotransmitter used in peripheral sensory neurons and is a primary excitatory neurotransmitter and neuromodulator within the central nervous system (CNS). The receptors that facilitate synaptic transmission at cholinergic synapses and beyond are divided into two broad subtypes: the ionotropic nicotinic acetylcholine receptors (nAChRs) and the metabotropic muscarinic acetylcholine receptors (mAChRs). This receptor classification is shared in both mammals and insects; however, both the pharmacological and functional characterization of these receptors within the Drosophila nervous system has lagged behind its mammalian model counterparts. In order to identify the impact of ACh receptor subtypes in regulating the performance of select neural circuits within the larval CNS, we have used a behavioral and electrophysiological approach to assess cholinergic modulation of locomotion, feeding, and sensory-CNS-motor (sensorimotor) circuit activity. We have exposed intact 3rd instar larvae to ACh agonists and antagonists to observe modulation of these behaviors and also expose an intact nervous system directly to solutions containing these compounds to address their influence on sensorimotor circuit efficacy. We reveal that chronic ACh exposure enhances locomotion but reduces feeding behavior and acute application excites a sensorimotor circuit. Nicotine exposure reduces activity through suspected rapid receptor desensitization. Moreover, chronic muscarine exposure reduces locomotion and feeding, but acute exposure enhances sensorimotor circuit activity. These results suggest a role for both nAChRs and mAChRs in modulating these select circuits and illuminates important pharmacological properties of cholinergic receptor subtypes in vivo. Funding Dept. of Biology, UK. Ribble funds (ES), Kentucky Science and

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